REMARKS

This paper is filed in response to the official action dated September 24, 2004. This paper is timely-filed as it is accompanied by a petition for an extension of time to file in the third month and a check covering the requisite extension fee of $1020.

Claims 1-49 are pending, but claims 6, 8, 9, 18, 19, 22-25, 30-32, 36-47, and 49 have been withdrawn from further consideration pursuant to Applicant's provisional election of a binding pair combination wherein ftsZ is the first molecule and GTP is the binding partner.[1] Therefore, claims 1-5, 7, 10-17, 20, 21, 26-30, 33-35, and 48 are presently at issue.

By the foregoing, claims 10-12, 23, 26, 28, and 33-35 have been amended. Support for the amendments may be found throughout the application and in the claims as originally filed. No new matter has been added.

The examiner stated that "the phrase 'α/β domain structure' is interpreted to mean a domain comprising alpha helix and beta sheet structures...." *See* official action at page 2. Applicant agrees that the examiner has accorded the correct meaning to this limitation, which is used consistently throughout the application and pending claims.

Claims 1-7, 10-17, 20, 21, 26-29, 33-35, and 48 have been rejected under 35 U.S.C. §112, first paragraph, as assertedly failing to comply with the written description requirement.[2] Claims 26-29 have been rejected under 35 U.S.C. §112, second paragraph, for insufficient antecedent basis. Additionally, claims 1, 4, 5, 7, 10, 13-17, 20, 21, 26, 27, 33-35, and 48 have been rejected under 35 U.S.C. §102(b) as assertedly being anticipated by Yu *et al.*, "Ca^{2+}-mediated GTP-dependent dynamic assembly of bacterial cell division protein FtsZ into asters and polymer networks *in vitro*," *EMBO J., 16(17):*5455-5463 (1997) (hereafter, "Yu *et al.*").

Claim 23 has also been objected to as being of improper form. Claim 23 has been amended to depend from claim 22, and therefore this objection has been overcome and should be withdrawn.

The specification has been objected to as containing sequence listings which are not properly identified. The specification has been amended to include a substitute sequence listing including the amino acid sequence of the LFA-1 I domain (SEQ ID NO:

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[1] Claim 6 has been withdrawn (by the applicant) as directed to a non-elected species; additionally, claim 23 has been amended to depend from withdrawn claim 22, and therefore should also be withdrawn.

[2] As previously noted, claim 6 has been withdrawn.

35), and the full length amino acid sequence of LFA-1 (SEQ ID NO: 36). Therefore, this objection to the specification has been overcome and should be withdrawn.

Finally, the specification has been objected to as failing to include a brief description of the drawings. The specification has been amended to include a brief description of the drawings, and therefore this objection to the specification has also been overcome and should be withdrawn.

The various bases for the claim rejections are addressed below in the order presented in the official action. Reconsideration of the application, as amended and in view of the following remarks, is solicited.

CLAIM REJECTIONS – 35 U.S.C. §112, FIRST PARAGRAPH

Claims 1-7, 10-17, 20, 21, 26-29, 33-35, and 48 have been rejected under 35 U.S.C. §112, first paragraph, as assertedly failing to comply with the written description requirement. Applicant traverses the rejections and respectfully submits that claims 1-7, 10-17, 20, 21, 26-29, 33-35, and 48 are supported by an adequate written description.

The examiner recognized that the application "describes working examples of 9 proteins," but asserted that the "9 species of proteins described do not adequately describe the generic claims." *See* official action at page 5. The examiner further asserted that "[d]escription of methods using 9 proteins in the specification does not comprise a representative number of the undefined large genus of claimed methods." *Id.*

Moreover, with regards to the elected species of ftsZ, the examiner alleged that:

> the specification does not describe an allosteric site in FtsZ, or effectors of any type of FtsZ. The specification does not describe the Rossman fold structure of FtsZ. ... The specification does not describe a method utilizing FtsZ that comprises effectors, or the claimed structural limitations of FtsZ such as Rossman folds, or the claimed structural and functional limitations of the effector such as increasing or decreasing binding or enzymatic activity....

See official action at pages 5-6.

Statutory law requires that the specification shall contain a written description of the invention. *See* 35 U.S.C. § 112, first paragraph. The courts have interpreted that provision as requiring that the description of the invention be sufficient to allow one of skill in the art to recognize that the applicant was in possession of the subject matter claimed. Vas-Cath v. Mahurkar, 935 F.2d 1555 (Fed. Cir. 1991); *accord*, M.P.E.P. §

2163 (I). Possession is shown by describing the claimed invention with all of its limitations using descriptive means such as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown by describing an actual reduction to practice or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention. *See, e.g.*, M.P.E.P. § 2163 (I).

In the "Summary of the Invention," Applicant provides the following description of the claimed subject matter:

> ...the present invention provides methods of modulating binding interaction between a first molecule which is not LFA-1 or an I domain-containing fragment thereof, and a binding partner molecule, said first molecule comprising an α/β domain structure, said α/β structure comprising an allosteric regulatory site, said method comprising the step of contacting said first molecule with an allosteric effector molecule that interacts with said allosteric regulatory site and promotes a conformation in a ligand binding domain of said α/β structure that modulates binding between said first molecule and said binding partner molecule.

See application at page 3, line 28 – page 4, line 4.

The application discloses a large number of proteins that include an α/β domain structure (*see* Table I) and also teaches how to identify proteins including such a domain for use in the claimed methods, as demonstrated, for example in Table 3 (*see* Example 1). Each α/β protein includes common structural features, *i.e.*, each includes an α/β domain structure comprising alpha helix and beta sheet structures. Additionally, most α/β domain structures include a Rossman or Rossmann-like fold. In this regard, the application specifically teaches that Rossman or Rossmann-like folds are found in many members of the alpha/beta domain superfamily:

> [m]any members of the [alpha/beta domain] superfamily, including proteins comprising an integrin I domain, von Willebrand factor comprising A domain structures, and various enzymes, have an open twisted beta sheet which gives rise to a fold in the protein's three dimensional structure. This fold is commonly referred to as a Rossmann fold, a Rossmann-like fold, or a dinucleotide binding fold.

See application at page 1, lines 22–26.

The aforementioned common structural characteristics of α/β proteins corroborate Applicant's possession of the claimed genus as of the application filing date. *See, e.g.*,

M.P.E.P. § 2163 (I). In view of the aforementioned application teachings, which provide distinguishing identifying characteristics for the proteins used in the claimed genus, it is respectfully submitted that one of ordinary skill in the art would recognize that Applicant was in possession of the necessary common attributes or features possessed by α/β proteins for use in the claimed methods.

Applicant also described the actual reduction to practice of at least 21 α/β protein/binding partner molecule combinations for use in the claimed methods, and these 21 α/β protein/binding partner molecule combinations include more than nine protein species recognized by the Examiner (*see* official action at page 5). For example, Example 3 describes modulating CD11b binding to both ICAM-1 and iC3b; Example 4 describes modulating C2 binding to C4b and Factor B binding to C3b; Example 9 describes modulating $\alpha_E\beta_7$ binding to E-cadherin, $\alpha_v\beta_3$ binding to vitronectin, $\alpha_4\beta_1$ binding to VCAM, $\alpha_d\beta_2$ binding to VCAM, $\alpha_L\beta_2$ binding to ICAM-1, $\alpha_M\beta_2$ binding to iC3b, and $\alpha_4\beta_7$ binding to MAdCAM-1; Example 11 describes modulating $\alpha_2\beta_1$ binding to collagen and $\alpha_7\beta_1$ binding to VCAM; Example 12 describes modulating alpha 1 binding to collagen; Example 15 describes modulating von Willebrand factor binding to gpIb; Example 16 describes modulating CD11b binding to ICAM-1; Example 17 describes modulating Rac1 binding to GTP; Example 18 describes modulating DapB binding to NADH, ENR binding to NADH, ERA-GTPAse binding to GTP, and yihA binding to GTP; and, Example 19 describes modulating HPPK binding to ATP. In view of these exemplified proteins, which each possess the distinguishing identifying characteristics discussed above, it is respectfully submitted that one of ordinary skill in the art would recognize that Applicant was in possession of the necessary common attributes or features possessed by α/β proteins for use in the claimed methods.

With respect to the elected species of ftsZ, Applicant reduced to practice modulation of ftsZ binding to GTP in Example 20. Additionally, the application discloses that ftsZ is an α/β protein, and therefore the application teaches that ftsZ likely includes a Rossmann or Rossman-like fold, as explained previously. Moreover, original claim 48, which is (a multiple dependent claim) dependent on claim 5, recites that ftsZ comprises an allosteric regulatory site and a Rossman fold structure. Furthermore, Table 3 in Example 1 includes data predicting that ftsZ includes an allosteric site based on the structural relatedness between ftsZ and molecules known to possess an allosteric site. The application further explicitly discloses that a Rossmann fold structure comprises an

allosteric regulatory site (*see, e.g.*, application at page 9, lines 15-16). Thus, the application teaches that ftsZ includes an allosteric site and a Rossman fold structure.

Applicant also disclosed that the claimed methods use effector molecules such as diaryl compounds, more preferably diaryl sulfide compounds and diarylamide compounds, and most preferably diaryl sulfide compounds. *See* specification at page 15, lines 2-9. The application discloses numerous specific diaryl compound structures. *See, e.g.*, specification at Table 2. Thus, the application discloses effector molecules of ftsZ.

For all of the foregoing reasons, Applicant submits that the claimed subject matter is supported by an express description of the full scope of the invention and one of skill in the art would recognize that Applicant possessed that subject matter at the time of filing. Accordingly, the rejection of claims 1-7, 10-17, 20, 21, 26-29, 33-35, and 48 as lacking written description has been overcome and should be withdrawn.

CLAIM REJECTIONS – 35 U.S.C. §112, SECOND PARAGRAPH

Claims 26-29 have been rejected under 35 U.S.C. §112, second paragraph, for assertedly insufficient antecedent basis. Applicant traverses the rejections.

Claims 26 and 28 have been amended to correct the asserted antecedent basis problem. It is respectfully submitted that the asserted lack of antecedent basis in claims 26-29 did not render these claims indefinite under §112, because a claim is considered definite as long as "the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." *See* M.P.E.P. § 2173. Nevertheless, in view of the amendments to claims 26 and 28 presented herein, the rejections of claims 26-29 for indefiniteness should be withdrawn.

CLAIM REJECTIONS -- 35 U.S.C. §102

Claims 1, 4, 5, 7, 10, 13-17, 20, 21, 26, 27, 33-35, and 48 have been rejected under 35 U.S.C. §102(b) as assertedly being anticipated by Yu *et al.* Applicant respectfully traverses the rejections.

It is well-established that each and every limitation of a claimed invention must be present in a single prior art reference in order for anticipation to occur. *See*, for example, *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1349 (Fed. Cir. 1998). The standard for anticipation is one of strict identity. This standard has not been satisfied with respect to claims 1, 4, 5, 7, 10, 13-17, 20, 21, 26, 27, 33-35, and 48.

Yu *et al.* discloses that "[i]ncreasing the Ca^{2+} concentration from 0.1 to 40 mM resulted in a reproducible increase in GTP binding by FtsZ." Yu *et al.* further discloses

that "GTPase activity of FtsZ was stimulated at low Ca^{2+} concentrations, but inhibited at higher Ca^{2+} concentrations."

Yu *et al.* does not disclose an effector molecule capable of modulating the binding interaction between ftsZ and GTP, as recited by all pending claims. Rather, Yu et al. discloses that Ca^{2+} is capable of modulating such binding interaction. Ca^{2+}, as is understood in the art, is an "atom," and an atom is *merely* a component of a molecule, which by definition includes at least two atoms. Yu *et al.* therefore does not disclose or suggest contacting ftsZ with an allosteric effector *molecule* capable of modulating the binding interaction between ftsZ and GTP, as recited by all pending claims. Moreover, Yu *et al.* does not disclose or suggest a ftsZ allosteric site that can accommodate the effector molecule recited by all claims. Accordingly, Yu *et al.* does not disclose each and every limitation for a method of modulating GTPase activity of ftsZ with a molecule.

For the reasons set forth above, it is respectfully submitted that the outstanding anticipation rejections of claims 1-7, 10-17, 20, 21, 26-29, 33-35, and 48 have been overcome and therefore should be withdrawn.

CONCLUSION

It is submitted that the application is in condition for allowance. Should the examiner wish to discuss any matter of form or procedure in an effort to advance this application to allowance, he is respectfully invited to telephone the undersigned attorney at the indicated telephone number.

Respectfully submitted,

MARSHALL, GERSTEIN & BORUN LLP

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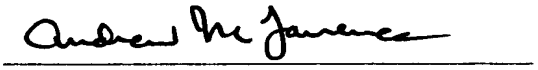
By: 

Andrew M. Lawrence, Reg. No. 46,130
Attorney for Applicant
6300 Sears Tower
233 South Wacker Drive
Chicago, Illinois 60606-6357
(312) 474-6300